Modeling Hepatitis A Transmission in the United States

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Objective of the model

Evaluate the impact of different immunization strategies on the evolution of Hepatitis A (HAV) infection over time in the U.S., using a dynamic mathematical model.

The model accounts for

- herd protection induced by vaccination
- HAV importation

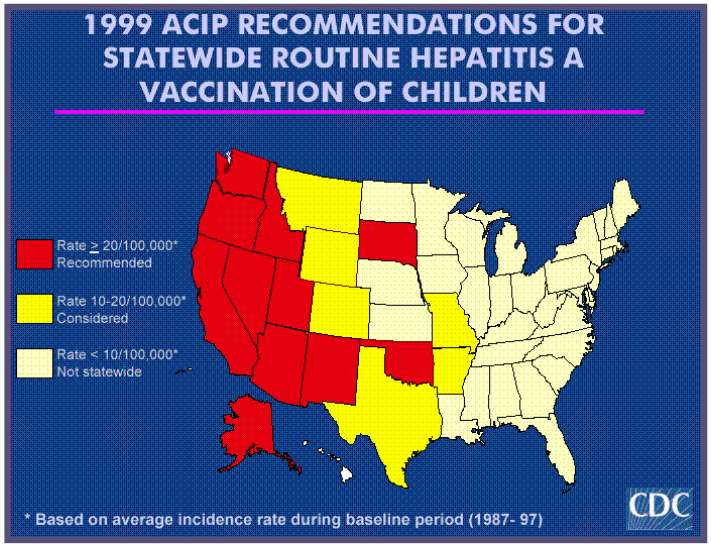
Roadmap

- The model
- Project the impact of age of immunization on herd protection effects
- Project the impact of nationwide versus regional (ACIP 1999) immunization strategies
- Project the impact of immunization at age 2 versus age 12 years
- Potential for spread and elimination of HAV
- Conclusions

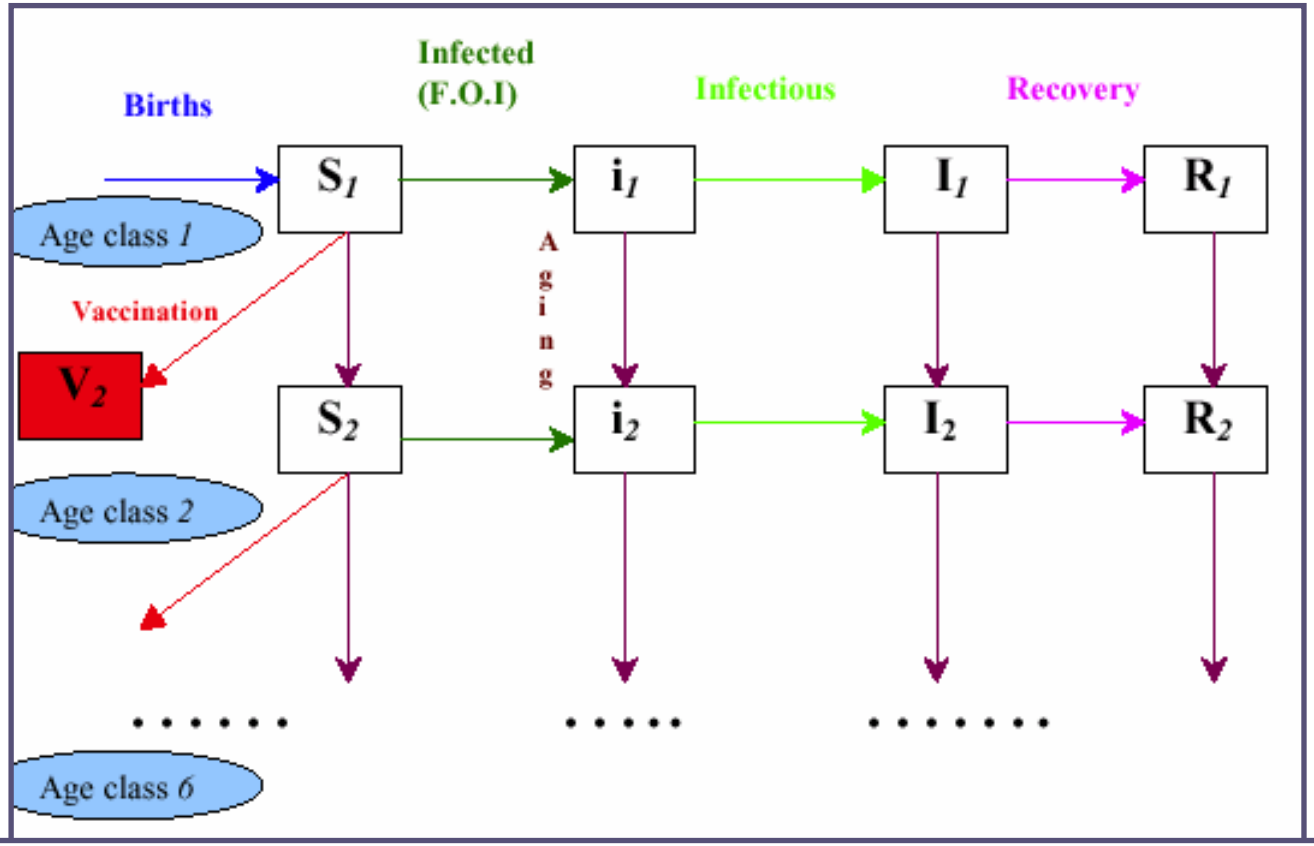
The model

- Dynamic “compartmental” model describing passage of hosts through the different “infectivity stages” of HAV:
  - Susceptible
  - Infected not yet infectious
  - infectious
  - Recovered - Immune
  - Vaccinated

- Stratified by age and geographic regions
  - Six age classes:
    0-1, 2-5, 6-11, 12-19, 20-39, 40+ (years)
  - Regions: as defined in
    ACIP 1999 recommendations
    based on HAV incidence rates
    at that time



The model



Infectivity stages:

S: Susceptible **i**: Infected & not yet infectious **I**: Infectious

R: Recovered-Immune **V**: Vaccinated

Assumptions and Sources of Key Parameters

"Force of infection" (F.O.I) = per-susceptible rate of acquisition of the infection:

- Age-dependent
- Based on incidence pre-vaccination, adjusted for
  - susceptibility [*NHANES III seroprevalence*]
  - under-reporting
  - asymptomatic infection
- FOI changes with time as prevalence of infectious hosts changes (to reflect herd protection)

Assumptions and Sources of Key Parameters (continued)

- Vaccine coverage
  - In 2001 (cumulative coverage for 2-18 yr olds): ACIP regions 1, 2, 3= 30%, 20%, 1%

    [*Samandari, Bell, Armstrong (2004)*]
  - After 2001 (for every vaccinated cohort):

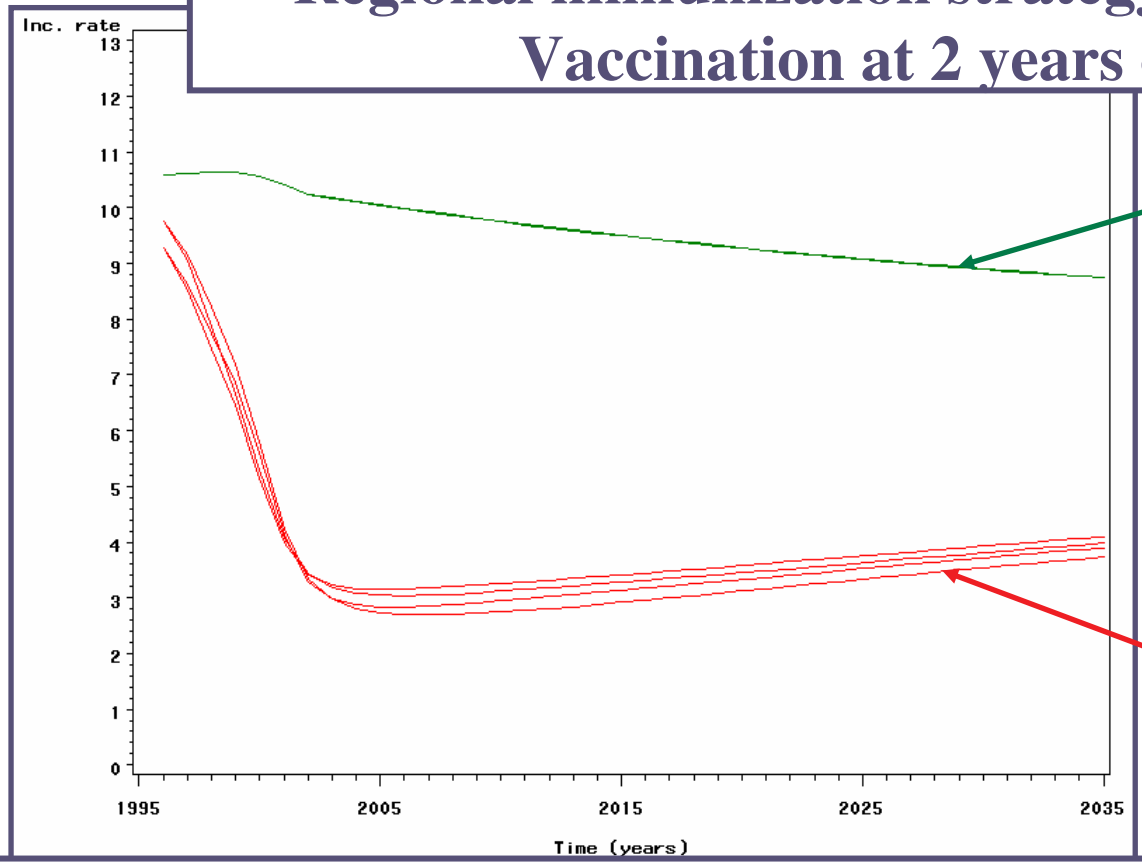
    70% assuming 100% efficacy

    or 78% assuming 90% efficacy

- Vaccine efficacy assumed to last at least 25 years

A static model underestimates the benefits of immunization: need for a dynamic model

Regional immunization strategy (ACIP 1999)
Vaccination at 2 years of age



Not accounting for herd protection (static model)

Accounting for herd protection (dynamic model)

US reported incidence rates are in line with
Predictions of dynamic model:
- **2001: 3.8 / 100,000**
- **2003: 2.7 / 100,000**

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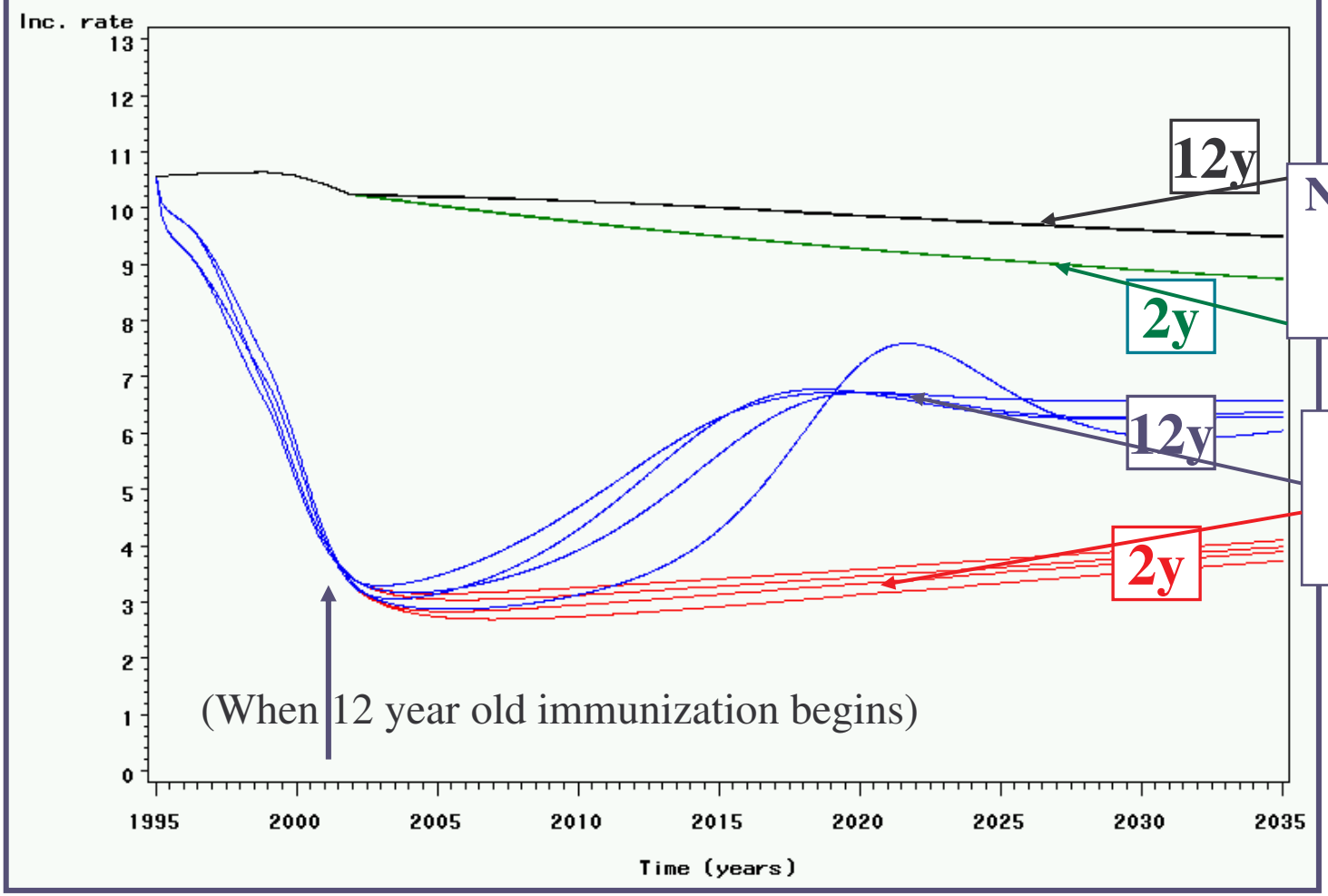
Herd protection effects of immunization more important with vaccination at age 2 than age 12 years

Regional immunization strategy (ACIP 1999)



Not accounting for herd protection (static model)

Accounting for herd protection (dynamic model)

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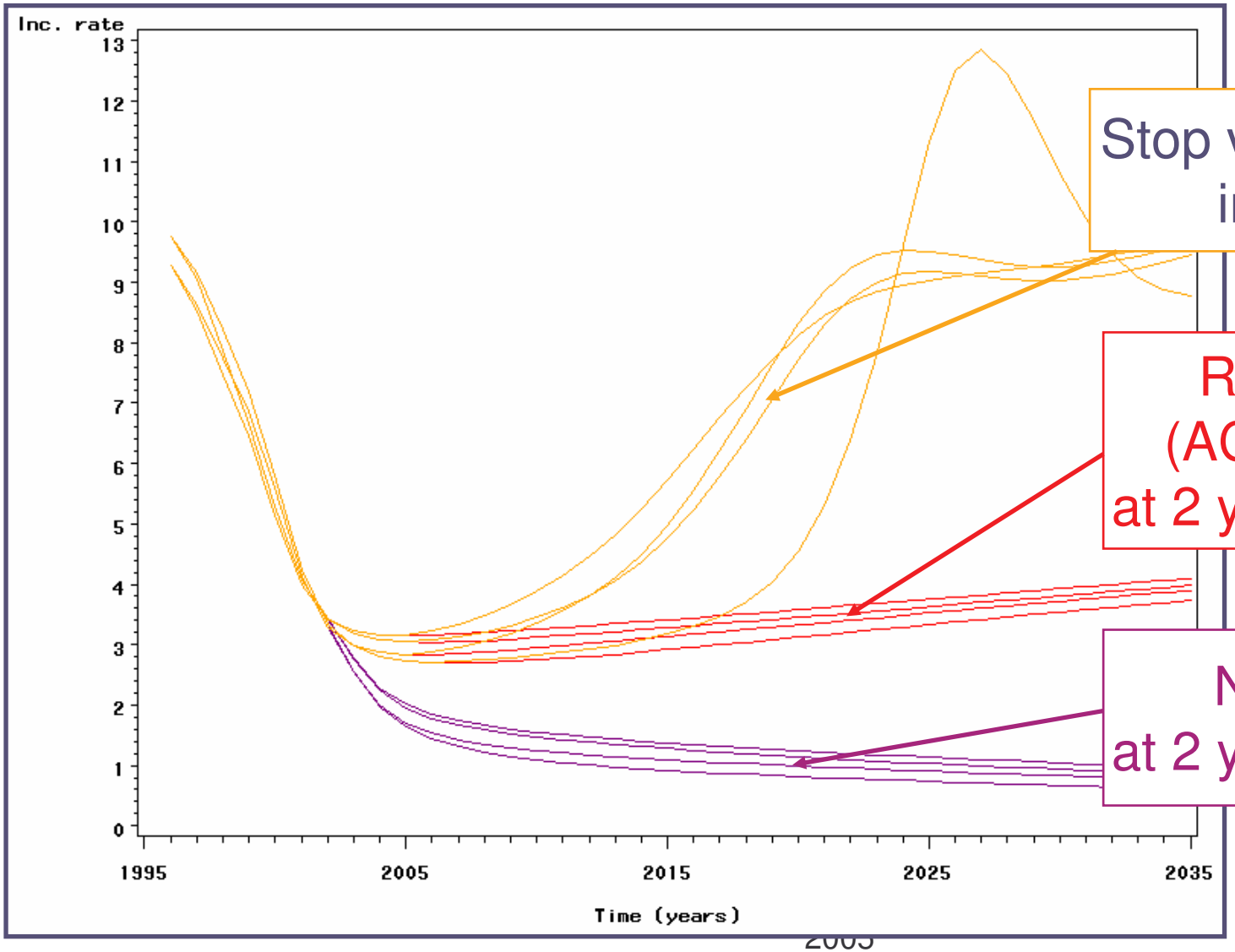
Incidence rates for the whole US Immunization at 2 years of age with different immunization strategies



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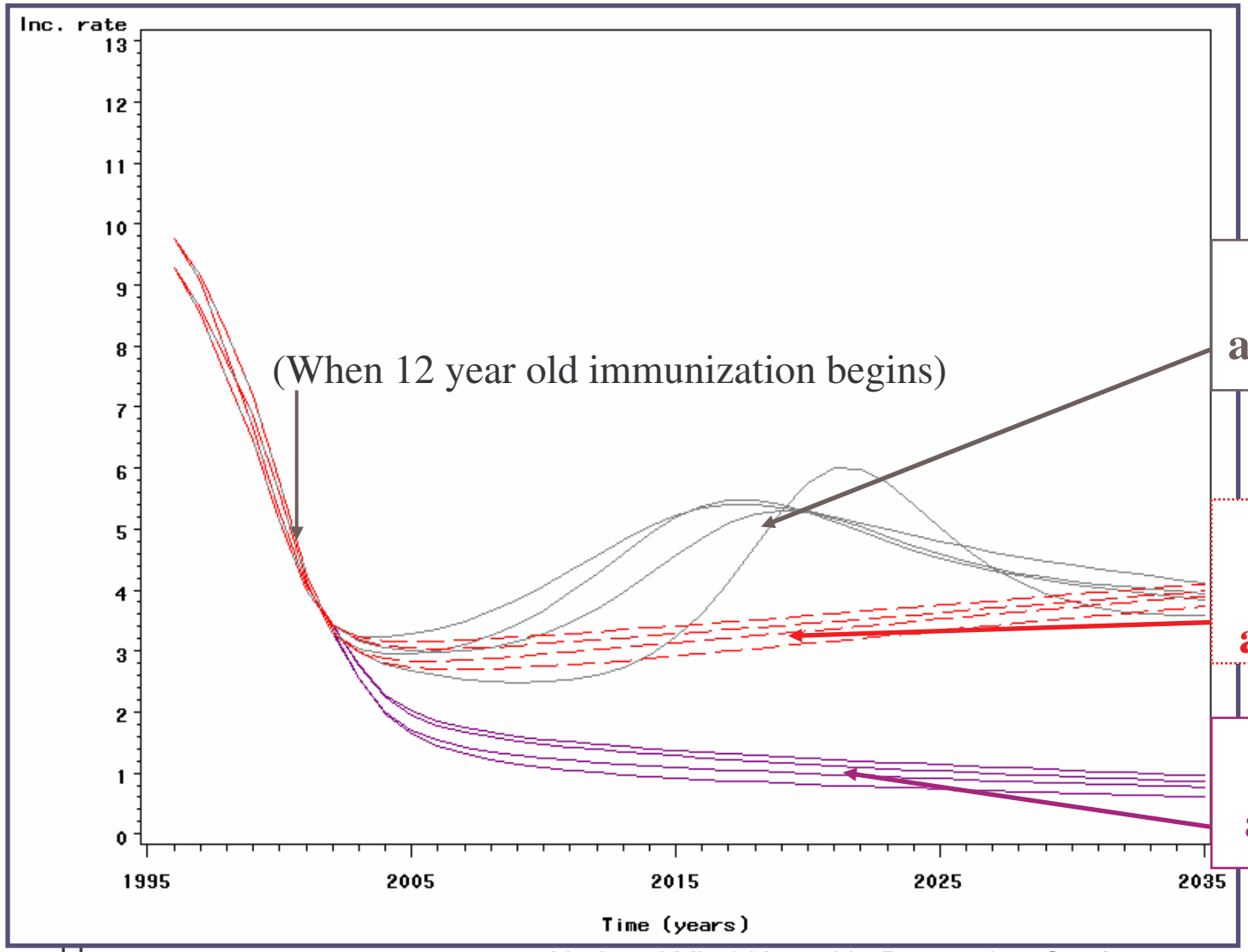
Incidence rates for the whole US with different immunization strategies



National
at 12 years of age

Regional
(ACIP 1999)
at 2 years of age

National
at 2 years of age

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HAV cases predicted by the model with the different immunization strategies

Period	Predicted cases		
	Regional strategy (ACIP 1999) at 2 years of age	Nationwide immunization at 2 years of age (% reduction)	Nationwide Immunization at 12 years of age (% reduction)
2002-2009	181,000	158,000 (-13%)	182,000 (+ 1%)
2002-2019	261,000	188,000 (- 28%)	296,000 (+ 13%)
2002-2029	351,000	212,000 (- 40%)	416,000 (+ 19%)

Potential for spread and Elimination of HAV

- Evaluated by estimating the *basic reproduction number* "R_0"
- R_0 = mean number of secondary infectious cases generated by 1 primary infectious case introduced into a totally susceptible population.

- **Estimate of Hepatitis A R_0 from the model: 1.1 – 1.6**
- compares with R_0 estimates of 5 for smallpox, 4 – 7 for Mumps, 6 – 7 for Diphtheria and Rubella and 12 - 18 for Measles.

Low R_0 for HAV very conducive to disease elimination.

- To achieve HAV ELIMINATION in the USA…
  - A minimum of **40%** of 2 year olds require immunization in the absence of any HAV importation!
  - A higher coverage is needed to avoid outbreaks due to HAV importation
  - 70% coverage would bring incidence to low levels

Conclusions

- Herd protection is a crucial aspect of transmission
- Immunization at 2 years of age provides more herd protection than immunization at 12 years of age
- Regional strategy (ACIP 1999) may lead to plateauing and even a slow rise in HAV disease
- Nationwide routine immunization at 2 years of age would be most beneficial compared to regional “ACIP 1999” strategy
- A nationwide routine program at 12 years of age is predicted to result in more HAV disease than the regional “ACIP 1999” strategy at 2 years of age.
- The model predicts that national immunization at 2 years of age leads to 40% decrease in incidence by 2029 compared to regional strategy